



A RETROSPECTIVE STUDY OF INCIDENTAL GALLBLADDER CARCINOMA IN A TERTIARY CARE CENTRE IN NORTH EAST INDIA

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Myrthong****ABSTRACT**

Background: Cholecystectomy is performed routinely for benign gallbladder for acute or chronic cholecystitis due to various causes with cholelithiasis being the most common cause. Incidental malignant diseases of gallbladder are encountered infrequently in patients undergoing cholecystectomy. This may be discovered intra-operatively by frozen section study or post-operatively when the histopathological reports arrive. This retrospective study was undertaken to determine the prevalence of all incidental gallbladder carcinoma in pre-operatively unsuspected gallbladder specimens. **Material and methods:** The retrospective study was undertaken by searching the departmental pathology database on gallbladder specimens who had undergone routine cholecystectomy for benign gallbladder disease during the study period (January 2015 to April 2026). A total of 2293 cholecystectomies performed across the study period were included for analysis. Only cases with no preoperative clinical or radiological findings regarding malignancy were included. Data included patient age and gender, preoperative clinical diagnosis, radiographic findings, intra-operative characteristics of gallbladder and pathologic staging were studied from the patient files. **Results:** Of the 2293 cholecystectomy records retrieved, 29 (1.26%) were found to have incidental gallbladder adenocarcinoma and 1 was adenocarcinoma in situ. Chronic cholecystitis was the most frequent pre-operative diagnoses and gallstones were associated in approximately 90% of patients. There was female predominance and frozen section was helpful with specificity of 100%. **Conclusion:** Thorough routine histopathological examination of gallbladder specimens done for benign gallbladder diseases is important to provide an early diagnosis and timely management.

KEYWORDS : Carcinoma, gallbladder, incidental,**INTRODUCTION:**

Incidental gallbladder carcinoma (IGBC), also known as occult, missed or in-apparent gallbladder carcinoma (GBC) is defined as carcinoma of gallbladder detected during or after cholecystectomy done for benign gallbladder diseases. [1] The incidence of IGBC in routine cholecystectomy specimens ranges from 0.3% to 2%. [2] Pre-operative radiological or intraoperative suspicion for malignancy is usually not present in these patients. [3,4] Gallstones are associated in 75%-90% of cases of GBCs.[5] Other risk factors include calcified gallbladder wall, adenomatous polyp, choledochal cyst, oestrogen, obesity, chemical carcinogens, etc. [6] As per the Indian Cancer registry, highest incidences of GBC in India have been reported from New Delhi and Bhopal and lowest incidence from Chennai. [5] This study was undertaken to find the incidence of IGBC in patients undergoing cholecystectomy for various benign conditions of gallbladder in patients from North Eastern part of India as there are limited data available from the region.

Material and methods: The study design was retrospective record-based study and the study period was from January 2015 till April 2026. Histopathological data of all gallbladder specimen of the department of general surgery during the study period was retrieved. The patient files of those patients diagnosed with gallbladder carcinoma were then retrieved from the medical records department of the hospital and various patient parameters recorded. From those cases, only cases with no prior suspicion of malignancy were included. The inclusion criteria included cases of incidental gallbladder carcinoma in histopathological reports of cholecystectomy specimens for benign gallbladder diseases.

Exclusion criteria included those cases of carcinoma gallbladder where preoperative radiological suspicion of malignancy was suspected. The demographic and clinical data on patient's age, gender, preoperative diagnosis, radiological findings, intra-operative findings and post-operative outcome measures were retrieved from the files.

American Joint Committee on Cancer staging of the cases were also recorded. Ethical clearance was not obtained for the study as it was purely a retrospective record-based study with no disclosure of patient details. Data was collected and entered in Microsoft Excel sheet (Microsoft Corporation, Redmond, WA), and statistical analyses performed using IBM SPSS Statistics for Windows, Version 25 (IBM Corp, Armonk, NY).

RESULTS:

A total of 2293 cholecystectomies were performed during the study period for benign gallbladder diseases, 29 (1.26%) of which were diagnosed as gallbladder carcinoma. The various pathological diagnoses of the cholecystectomy specimens have been shown in Table 1. Chronic cholecystitis was the most common histopathological diagnosis (1685, 73.48%). Mean age of the patients diagnosed with IGBC was 61 ± 9.21 years. There was female predominance with a ratio of $\approx 4:1$ in relation to males as shown in Table 2. Cholelithiasis (18, 62.07%) was the most common pre-operative diagnosis in the patients with IGBC followed by chronic cholecystitis (14, 48.28%) as shown in Table 3. Per-operative 26 (89.66%) patients had associated gallstones. Intra-operative frozen section was sent in 8 patients, 5 (17.26%) of which turned out to be positive for malignancy for which radical cholecystectomy along with lymphadenectomy were performed as shown in Table 4. Chronic cholecystitis was diagnosed in the remaining 3 cases. For the remaining 24 patients, gallbladder carcinoma was diagnosed post-operatively and radical cholecystectomy with lymphadenectomy were performed subsequently in 20 patients. In 4 patients, no further surgeries were performed in consultation with the patients as they had T1a diseases. One patient was diagnosed as having carcinoma in situ. Most patients were found to have stage T1b disease followed by T2 and T1a as shown in Table 5.

Table 1 showing the various histopathological diagnoses of cholecystectomy specimens

Pathology of gallbladder specimen	Numbers (n=2293)	Percentage
Chronic cholecystitis	1685	73.48
Cholesterosis	258	1.25
Pyloric metaplasia	134	5.84
Xanthogranulomatous cholecystitis	62	2.70
Intestinal metaplasia	36	1.57
Gallbladder carcinoma	29	1.26
Mucocele of gallbladder	27	1.18
Adenomyomatosis	15	0.65
Acute cholecystitis	13	0.57
Gallbladder polyps	11	0.48
Empyema of gallbladder	10	0.47
Normal gallbladder	7	0.30
Ectopic gastric and pancreatic tissue	2	0.09
Lymphoplasmacytic cholecystitis	2	0.09
Porcelain gallbladder	1	0.04
Carcinoma in situ	1	0.04

Table 2 showing the demographic characteristics of IGBC patients

Patient characteristics	n=29	%
Mean age in years $\pm$ SD	61 $\pm$ 9.21	
Male	6	20.69
Female	23	79.31

Table 3 showing the various pre-operative diagnoses of IGBC specimens

Preoperative diagnosis	n=29	%
Cholelithiasis	18	62.07
Chronic cholecystitis	14	48.28

Table 4 showing the various per-operative characteristics of IGBC specimens

Per-operative findings	n=29	%
Associated with gallstones	26	89.66
Thickened wall	5	17.24
Focal mass	2	6.90
Frozen section sent	8	27.59
Frozen section positive for malignancy	5	
Difficult cholecystectomy	10	34.48

Table 5 showing the various post-operative characteristics of IGBC specimens

Post-operative diagnosis	n=29	%
T1a	4	13.79
T1b	15	51.72
T 2	8	27.59
T 3	2	6.90
Well-differentiated	5	17.24
Moderately differentiated	10	34.48
Poorly differentiated	13	44.83
Signet ring-cell morphology	1	3.45
Lymph node involvement	3	10.34
Lympho-vascular invasion	4	13.79

DISCUSSION:

Both open and laparoscopic surgical approaches were included as the type of surgical approach did not correlate with survival rate of IGBC cases. [7] The mean age of IGBC patients in the present series was 61 $\pm$ 9.21 years, close to 63.8 years by Alabi et al. [8] and 58.6 years by Yadav et al. [9] However, Jha et al (49.14 years) [10] and Poudel et al (50.6 years) [11] reported much younger average age of patients with IGBC.

There was female predominance in the present study (79.31%) similar to previous studies by Yadav et al [9], Jha et al [10] Poudel et al [11] and Omhare et al, [12] which is likely due to estrogen increasing the risk of gallstone formation. [13]

The incidence of incidental gallbladder carcinoma in the present study was found to be 1.26%, which is higher than reported by Jha et al (0.41%), [10] and Gulwani et al (0.76%) [14] However, higher incidences of IGBC have been reported by Bhalla S, et al (1.74%), [13] Poudel et al (1.67%), [11] Omhare, et al (1.82%), [12] and Sangwan et al (1.90%), [15].

The present study found that most IGBC cases were associated with cholelithiasis (89.66%) similar to the reports by Yadav et al [9] and Gulwani et al [14].

The present study questions the accuracy of pre-operative radiological diagnosis of early-stage gallbladder cancer. In up to 70% of IGBC cases, initial imaging features resembled benign conditions like cholelithiasis or chronic cholecystitis. [13] Advanced imaging modalities, like contrast-enhanced ultrasonography (CEUS), MRI (diffusion weighted) along with tumour markers could and AI-driven image analysis, could increase the early detection of malignancy. [16,17]

Intraoperative frozen section protocol depending on suspicious features may result in timely interventions. [13] In the present study, intraoperative frozen section was done in 8 cases, and adenocarcinoma was detected accurately in 5 cases similar to Zhang WJ, et al. [18]

Poorly differentiated adenocarcinoma was the most predominant subtype in IGBC (44.83%) followed by moderately differentiated (34.48%) and well-differentiated (17.24%). However, Bhalla S, et al [13] reported well-differentiated adenocarcinoma to be the most common type (52.94%), and Saikia K, et al, [19] Jha et al, [10] and Gulwani et al [14] found moderately differentiated adenocarcinoma to be the most common type of IGBC.

Prognosis of gallbladder cancer depend largely on the stage of the disease with nearly 100% five-year survival rate for Tis and pT1a tumors by simple cholecystectomy to nearly 70% five-year survival rate for T2 tumors by radical cholecystectomy in IGBC diagnosis. [20] In this study, most cases were in the T1b stage (51.72%) followed by T2 (27.59%). Whereas, Bhalla S, et al [13] reported T2 (60.7%) being the most common, followed by T1 (35.29%).

It is still debatable whether routine histopathological examination is necessary for all cholecystectomy specimens done for benign gallbladder diseases. Some authors have indicated that routine histopathological examination of all gallbladder specimens removed for benign diseases is not necessary as the incidence of IGBC is low less than 1% and simple cholecystectomy is optimal treatment in most of such cases. [3, 21,22] However, the Royal College of Pathologists recommend routine histopathological examination of all cholecystectomy specimens, as significant pathology may be present with apparently normal gross morphology. [23] Wu X, et al [24] and Kallianpur AA, et al [25] also recommend routine histopathological examination of cholecystectomy specimens to detect gallbladder cancer early and improve survival for patients.

The limitations of the study include the retrospective nature and its reliability on available records with potential for incomplete data and selection bias. Follow-up study was not possible as patient data on follow-up visits were not available due to mostly outpatient nature of follow-up practices.

Conclusion: This retrospective record-based study has been able to put insights into the incidence and characteristics of IGBC in a tertiary care setting in North East India. It also highlights the limitations of presently available imaging armamentarium in the pre-operative setting and stresses on the role of routine histopathological examination of cholecystectomy specimens for early detection of IGBC. Improved diagnostic modalities and proactive surgical approach in suspicious gallbladder pathology could impact the overall management and survival of patients with IGBC. Prospective studies on advanced imaging modalities with molecular markers may validate these findings and support enhancements in preoperative screening.

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